IDIOPATHIC MEGAESOPHAGUS IN THE DOG: REASONS FOR SPONTANEOUS IMPROVEMENT AND A POSSIBLE METHOD OF MEDICAL THERAPY

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Introduction

Descriptions of idiopathic megaesophagus in the dog reveal a variable clinical picture. Reports of either presence or absence of achalasia are both common, severity of the disorder is inconsistent and improvement in the condition may be described. Although the disorder frequently appears in particular breeds or in related animals, sporadic cases are also reported. No specific medical therapy is available and surgical disruption of the lower esophageal sphincter has met with incomplete success (3, 4, 8, 11–13).

Sokolovsky has demonstrated again that spontaneous improvement can occur with time if the dogs are fed in an upright position (13). He also suggested from radiological studies that achalasia is probably not a feature of the condition, and that the lower esophageal sphincter may function normally. More recently, manometric studies have shown that the lower portion of the esophageal body has the capacity for peristaltic motor activity and that the lower esophageal sphincter is in fact functionally normal in dogs with idiopathic megaesophagus (5). Furthermore, these studies indicated that at least two abnormalities contribute prominently to the clinical picture seen: (a) a variable portion of middle and upper esophagus lacks contractile activity, and (b) swallowing frequently fails to produce motor activity within the functional portion of the esophageal body and sphincter. The severity of these abnormalities varies considerably from animal to animal and the abnormalities may improve with time. Another feature of interest was also described. Although the esophagus in dogs with megaesophagus did not show hypersensitivity to methacholine chloride, administration of this drug allowed motor activity to appear after a swallow in the previously nonfunctioning portion of the esophagus.

The present study was performed to outline the spontaneous improvement in motor abnormality in dogs with megaesophagus, to determine whether similar less-pronounced motor changes could be observed in apparently "normal" dogs, and to determine whether there is a reasonable basis for using a cholinomimetic drug as a possible method of medical therapy.

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Materials and Methods

Five dogs with idiopathic megaesophagus were studied for periods from two weeks to 24 months. (see Figures 2 and 3). The diagnosis was made from the clinical signs of persistent regurgitation of swallowed food along with radiological demonstration of megaesophagus in the absence of gastroesophageal reflux or vascular compression of the esophagus. There was one male German Shepherd (Dog K), two miniature Schnauzer litter-mates, one male (Dog S) and one female (Dog B), and one female Wire-Haired Fox Terrier (Dog P). The fifth affected animal was a male miniature Schnauzer (Dog A) born along with two normal mates and resulting from a brother-sister mating of the two original minature Schnauzers.

Three "normal" dogs were also studied. All were free of regurgitation of swallowed foods, and X-ray studies demonstrated clearing of the esophagus with peristaltic contractions and absence of megaesophagus, hiatus hernia or gastroesophageal reflux. Two female German Shepherd litter mates (Dogs D and L) unrelated to the achalasia dogs, were studied from the age of three weeks and until the animals were eight months of age. One male minature Schnauzer (Dog X), a litter-mate of the sixth achalasia dog was studied from the age of two weeks to 11 months.

The dogs were maintained on a standard ration of dry dog chow and water *ad lib*, and were trained to swallow conventional manometric recording tubes. After a 12 to 15 hour fast, the animals were positioned unrestrained on the left side for study. Belt pneumographs around the chest and neck monitored respiration and swallowing respectively and swallowing was induced by injecting a bolus of 2–5 ml of water into the pharynx through a separate tube. Manometric studies were performed with multilumen polyvinyl catheter assemblies with side openings. The tubes were continuously per-

fused with distilled water by a syringe pump at rates between 0.6 and 2.4 ml/min. At these perfusion rates, pressures to 55 mm Hg can be accurately recorded within 0.5 sec. Pressures were transmitted to external pressure transducers[1] and results graphed on a linear direct-writing ink recorder. Pressures in millimeters of mercury were read as the mean between inspiratory and expiratory deflections. The amplitude of an esophageal contraction was calculated as the difference between mean resting esophageal pressure and the peak pressure of the contraction. Each point on the graphs represents the mean of the amplitudes of at least four contractions. The mean contraction amplitudes of the abnormal dogs were compared to those of the "normal" controls and the T test used to determine the statistical significance between the means. The length of functioning esophagus was determined by withdrawing the recording system through the length of the esophagus with swallowing records obtained at each 1.0 cm interval. Motor activity of the esophagus was also observed by cine X-ray studies after instillation of barium into the esophagus through a tube.

For determination of the effect of a cholinomimetic drug on esophageal body motor activity, four pressure recording tips were positioned to span the body of the esophagus. After a ten to 15 minute control period urecholine was given subcutaneously in a dose of 0.1 mgm/kg and esophageal body activity was then monitored for a subsequent 15 to 20 minutes. The procedure was repeated on a second day substituting a saline injection in place of the urecholine. For each minute, values from two to six swallows were averaged.

Results

Figure 1 outlines the frequency with which esophageal body motor activity occurs following a swallow. A number of points are evident. First, at less than six months of age "normal" dogs (D and L) may show a low response to swallowing approaching 60%. However, after six months of age the "normal" asymptomatic dogs all had swallowing responses greater than 80%. Second, symptomatic dogs with megaesophagus all had swallowing responses less than 60% whether younger or older than six months of age (Dogs A, K, P and B). When Dogs S and A with megaesophagus became asymptomatic, their swallowing responses increased to greater than 60%. Third, frequency of

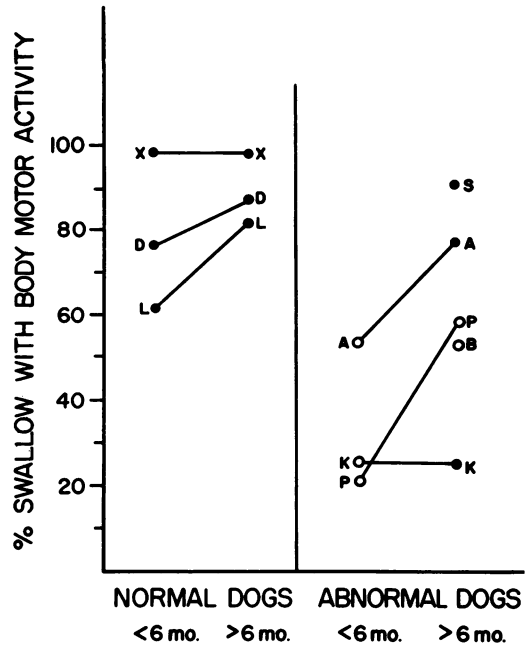

FIGURE 1. Percent response of esophageal body to swallowing in control and megaesophagus dogs. ○ – symptomatic dogs with megaesophagus on X-ray. ● – asymptomatic dogs with normal X-ray. Each dog is identified by a letter.

the esophageal body motor response to swallowing can improve with age and this is noted both in dogs with megaesophagus and in apparently asymptomatic "normal" dogs. Therefore the presence or absence of clinical signs and X-ray findings of megaesophagus related grossly to the swallowing response. However, Dog K who maintained a poor response to swallowing of 21% became completely asymptomatic with X-ray absence of megaesophagus after six months of age. In this animal, it seemed likely that other factors such as amplitude of the contraction wave and the length of the nonfunctioning segment of esophagus also contributed to the clinical picture of megaesophagus.

The amplitudes of the pressure peaks produced by esophageal contractions in the lower 5 cm of the esophageal body are graphed for each dog in Figure 2. Again, a number of features are apparent. First, "normal" dogs tended to have greater contraction pressures than abnormal dogs. Second, except for Dog K, the amplitude of the contraction waves was remarkably constant for each dog, including the "normals", over periods as long as 18 to 21 months. Dog K, initially severely symptomatic with marked megaesophagus on X-ray showed a continuous increase in contraction amplitude over the period of study and this increase paralleled his clinical improvement. Prior to nine

[1]Sanborn 267A, Hewlett-Packard Co., Waltham, Massachusetts.

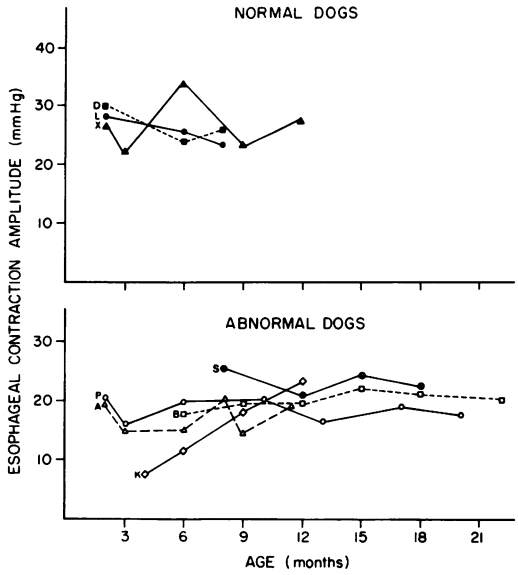

FIGURE 2. Esophageal contraction amplitude in control and megaesophagus dogs. Each dog is identified by a letter.

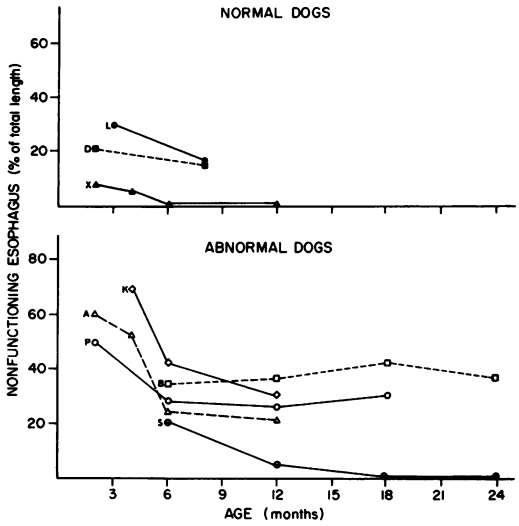

FIGURE 3. Length of nonfunctioning esophageal segment in control and megaesophagus dogs. Each dog is identified by a letter.

months, the contraction amplitudes for Dog K were significantly lower than normal ($p<0.001$) and at all times up to 12 months, contraction amplitudes were similarly significantly less than controls ($p<0.001$) for Dogs A, B and P. At nine to 12 months of age the amplitudes of contractions for Dogs A and K were not statistically different from the "normals" and both of these dogs were free of clinical signs by this time.

Figure 3 demonstrates the changes with age

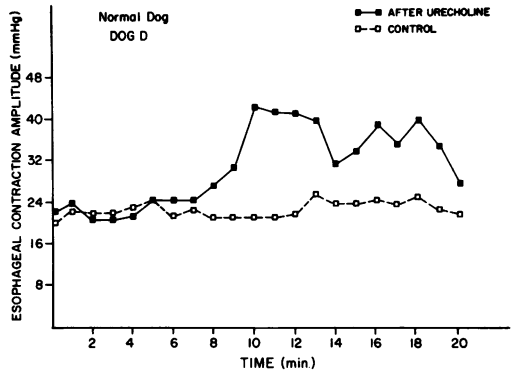

FIGURE 4. Lower esophageal contraction amplitude, after control saline injection and after urecholine 0.1 mgm/kg in a normal control dog.

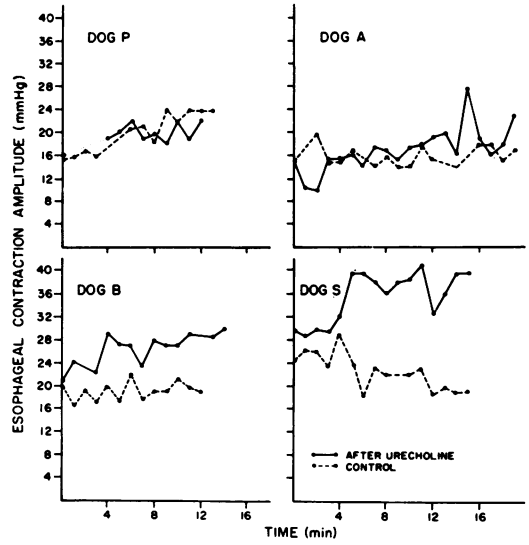

FIGURE 5. Lower esophageal contraction amplitude after a control saline injection and after urecholine 0.1 mgm/kg in four megaesophagus dogs.

in the length of the nonfunctioning portion of the esophagus. When first seen, the dogs with megaesophagus had 21 to 69% of the upper and/or middle esophagus nonfunctioning. However, continuous improvement occurred with return of function to a variable portion of this segment with time. The improvement was most dramatic during the first six months and maximum improvement was noted by 12 months of age. Furthermore, the apparently "normal" control dogs (D, L, and X) also demonstrated a small but definite nonfunctioning segment of upper esophagus when first studied. The abnormality improved with time in these dogs, as in the dogs with megaesophagus.

The effect of the cholinomimetic drug urecholine is shown in Figures 4 and 5 and Table I.

TABLE I

THE EFFECT OF URECHOLINE ON ESOPHAGEAL MOTOR ACTIVITY

	Swallowing Response[a]		Recording Tips with Motor Activity[b]	
	Before Urecholine	After Urecholine	Before Urecholine	After Urecholine
Normal Dog				
D	80	71	1, 2, 3, 4	1, 2, 3, 4
Abnormal Dogs				
P	46	33	2, 3, 4	1, 2, 3, 4
B	70	76	2, 3, 4	1, 2, 3, 4
S	77	70	3, 4,	2, 3, 4
A	58	64	2, 3, 4	1, 2, 3, 4
K	10	13	2, 3, 4	2, 3, 4

[a]Percent of swallows followed by an esophageal body motor response.
[b]Recording tips 5 cm apart in esophageal body; #1 most proximal and #4 most distal.

The frequency of response of esophageal body motor activity to swallows was not consistently altered by urecholine. In three animals there was a slight increase in the swallowing response following urecholine, and in three there was a slight decrease. However, urecholine did affect the amplitude of contractions in some of the dogs and the length of the nonfunctioning portion of the esophagus. There was an increase in amplitude of contractions in the control dog studied, beginning approximately seven minutes after injection of the drug. A similar response was seen in Dog S who had become completely asymptomatic by the time of this study. In Dogs A and B, whose motor function showed less improvement with age, the response was less evident. Dog P who remained clinically symptomatic with persistent megaesophagus, failed to demonstrate an increase of contraction amplitude following urecholine that was different from that following a saline injection.

In addition to an increase in contraction amplitude following urecholine, motor activity appeared in the previously nonfunctioning portions of the esophageal body (Table I). This was indicated by recording of a contraction wave in the more proximal tips that had failed to record motor activity prior to administration of the drug. More exact mapping of the degree of this improvement in the length of functioning esophagus was not performed.

DISCUSSION

The findings outlined in this report provide objective evidence of improvement in a number of parameters of esophageal motor function in dogs with megaesophagus. Improvement in the amplitude of contractions, and the frequency of the esophageal body motor response to swallowing along with a decrease in the length of the nonfunctioning portion of the esophagus accompanied clinical improvement of the animals. However, the severity of the abnormalities varied from animal to animal and the degree of improvement was also variable. These differences would suggest that the functional abnormalities may differ in different animals or breeds and that no one factor is necessarily responsible for clinical signs. A sufficient length of functioning esophagus with adequate amplitude of contractions will empty the esophagus even if the response to swallows is infrequent. Similarly, even though a significant portion of esophagus remains nonfunctioning, if most swallows produce a motor response of sufficient amplitude, the animal will appear to be normal. On the other hand, only moderate abnormality of all three parameters may produce clinical signs and megaesophagus. In the presence of a normally functioning sphincter and along with some motor activity, feeding animals in the upright position could provide adequate emptying of the esophagus until spontaneous improvement of motor activity occurs. If this improvement is sufficient, the dogs will become free of signs. If improvement does not reach adequate levels, signs will likely persist, perhaps indefinitely.

It is of interest that apparently "normal" control dogs may show abnormalities that are similar to, but less severe than those found in the megaesophagus dogs. Furthermore, these abnormalities also improve with time in the control dogs. This suggests that megaesophagus in dogs may represent developmental immaturity of innervation and/or musculature of the esophagus and that postnatal maturation may continue for up to 12 months to effect an

apparent improvement in the condition. It is likely that many factors, both hereditary and environmental could affect the maturation process and the clinical appearance of the disorder fits well with a polygenic or multifactorial inheritance pattern (1). This would explain the variable severity of the condition, the frequent appearance of the condition in littermates and related animals with a lack of any dominant or recessive inheritance pattern, and the unequal sex incidence.

The effect of a cholinomimetic drug on the dog disorder is also of interest, and suggests a possible mode of medical therapy. Although the frequency of motor activity to swallowing did not change, urecholine tended to improve the amplitude of contractions and to increase the portion of functioning esophagus. If a convenient route of administration is feasible, it seems reasonable that therapy with either an acetylcholine analogue or an anticholinesterase warrants a controlled clinical trial to assess its usefulness. It is possible that its administration might aid the spontaneous improvement or help maintain unimproved animals in an acceptable condition.

Two different mechanisms may be at fault to cause the abnormalities observed in dogs. Studies in dogs by Longhi and Jordan indicate that for an esophageal motor response to occur on swallowing, sensory reinforcement from the bolus in the esophageal lumen is required (10). A defect in this sensory reinforcement could explain the frequent absence of motor responses following swallows. On the other hand, the poor amplitude of contractions and absence of contractions in a portion of the esophageal body are more compatible with a defect in the motor pathways and exogenous administration of a cholinergic drug could facilitate these responses at many levels, either centrally or peripherally (6, 7, 9). Careful counts show normal numbers of myenteric ganglion cells in dogs with megaesophagus (4) and the muscle can apparently respond when adequately stimulated. Therefore the predominant abnormality in the motor pathway may be more centrally located.

Finally, the observations made in the present report again indicate that megaesophagus in the dog is not analogous to the disorder called Achalasia in humans. As suggested by Sokolovsky and recently confirmed by manometric studies, the lower esophageal sphincter functions normally in dogs with megaesophagus. Furthermore, the absence of hypersensitivity of the esophageal body to methacholine chloride[2] and the consistent improvement in the objective parameters of esophageal motor function are inconsistent with the findings in humans.

[2]Mecholyl, Merck & Co., Inc., Rahway, N.J.

Summary

Five dogs with idiopathic megaesophagus and three asymptomatic control dogs were studied serially for eight to 24 months by means of intraluminal esophageal manometry. Three esophageal motor abnormalities were observed in the dogs with megaesophagus: (a) esophageal contraction amplitude was lower than normal, (b) an esophageal body motor response was infrequent following swallows, and (c) a variable portion of the middle and/or upper esophagus failed to demonstrate motor activity. Over the first six to nine months of age, the dogs with megaesophagus demonstrated progressive return of function to the previously amotile portion of esophageal body, and an increase in the frequency of motor response to swallowing. One of the dogs with megaesophagus showed a progressive improvement in contraction amplitude. Improvement in these parameters of esophageal motor function was accompanied by clinical improvement. A similar, but less severe abnormality of motor function with subsequent improvement was also seen in two of the three asymptomatic control dogs. Administration of a cholinomimetic drug, urecholine, caused an increase in contraction amplitude and the appearance of motor activity in a portion of the previously nonfunctioning esophageal segment. Urecholine had no effect on the frequency of motor response to swallowing. These studies suggest that: (a) idiopathic megaesophagus in the dog is due to developmental immaturity of esophageal innervation and/or musculature, (b) postnatal maturation accounts for clinical improvement, and (c) administration of a cholinomimetic drug may provide a means of medical therapy for the condition.

Résumé

À l'aide d'un manomètre placé dans la lumière oesophagienne, on a effectué une étude d'une durée de huit à 24 mois sur cinq chiens souffrant de méga-oesophage, ainsi que sur trois chiens témoins asymptomatiques. On décela ainsi trois anormalités motrices de l'oesophage chez les chiens atteints de méga-oesophage, à savoir: a) une amplitude des contractions plus petite que normalement, b) une réponse motrice peu fréquente à la suite de déglutitions, et c) l'absence d'activité motrice dans une portion variable de l'oesophage supérieur et/ou moyen. Après avoir dépassé l'âge de six à neuf mois, les chiens souffrant de méga-oesophage

manifestèrent un retour fonctionnel progressif de la partie du tube oesophagien antérieurement privée de mobilité, ainsi qu'une augmentation dans la fréquence de la réponse motrice à la suite de déglutitions. Un des chiens atteints de méga-oesophage manifesta une amélioration progressive de l'amplitude des contractions. L'amélioration de ces paramètres de la fonction motrice de l'oesophage s'accompagna d'une amélioration clinique. On nota aussi une anormalité semblable mais moins prononcée de la fonction motrice, avec amélioration ultérieure, chez deux des trois chiens témoins. L'administration d'un médicament cholinomimétique, l'urécholine, amena une augmentation de l'amplitude des contractions et l'apparition d'activité motrice dans une portion du segment de l'oesophage antérieurement non fonctionnel. L'urécholine n'exerça aucune influence sur la fréquence de la réponse motrice à la suite de déglutitions. Les résultats de cette étude laissent supposer que: a) le méga-oesophage idiopathique du chien résulte d'une immaturité du développement de l'innervation et/ou de la musculature de l'oesophage; b) la maturation post-natale explique l'amélioration clinique; c) l'administration d'un médicament cholinomimémitique représenterait une approche thérapeutique de cette condition.

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